transferred to 264-935

MEMORANDUM

Subject: EPA Reg. No. 7501-42, Acute Mammalian Toxicity Review for Product Reregistration; DP Barcode D230645, Case# 030106

From: Mark J. Perry, Biologist [S] MJP
Precautionary Review Section 11/9/96
Registration Support Branch
Registration Division (7505W)

To: C.P. Moran, CRM
Special Review and Reregistration Division (7508W)

Applicant: Gustafson, Inc.
PO Box 660065
Dallas, TX 75266

FORMULATION FROM LABEL:

	% by wt.
Active Ingredient(s): Metalaxyl	28.35
Inert Ingredient(s):	71.65
Total:	100%

BACKGROUND

Gustafson Corporation has submitted previously reviewed acute oral, acute dermal, eye irritation and dermal irritation studies in support of reregistration of Apron-FL (EPA Reg. No. 7501-42). A more recent eye irritation study and new acute inhalation and dermal sensitization studies were also provided. The previously reviewed data was evaluated by the Agency on 11/8/83.

Apron-FL is a seed treatment fungicide intended for agricultural use which contains metalaxyl (28.35%) as the sole active ingredient. The subject acute studies were performed by Food and Drug Research, Product Safety Labs and Stillmeadow, Inc.; the assigned MRID/Accession numbers are 250989, 251408, 266162, 441168-02 and 441168-03.

IS Allegiance

RESULTS

1. Acute Oral (81-1); Category III

Due to insufficient dose level testing, the appropriate toxicity category cannot be determined from either acute oral study submitted in support of this product. As a result, both studies (acc. #s 250989 and 251408) are currently considered unacceptable. Additional acute oral studies are not needed, however, since the acute oral (rat) data referenced in the metalaxyl RED is considered adequate to allow classification of this product.

2. Acute Dermal (81-2); Category III

The original Agency review of this study (11/8/83) is considered valid. Quality Assurance and GLP statements were not requirements at the time this study was conducted.

3. Acute Inhalation (81-3); Category IV / Acceptable

4. Eye Irritation (81-4, Acc.# 266162); Category III / Acceptable

5. Dermal Irritation (81-5); Category II / Acceptable

The original Agency review of this study (11/8/83) is considered valid. However, due to the presence of grade 4 erythema on days 7 and 10, the assigned category has been changed from III to II. Quality Assurance and GLP statements were not requirements at the time this study was conducted.

6. Dermal Sensitization (81-6); Non-sensitizer / Acceptable

LABELING

1. The recommended signal word is "warning / aviso."

2. The recommended precautionary statements are as follows:

Causes skin irritation. Harmful if swallowed or absorbed through skin. Causes moderate eye irritation. Do not get on skin or on clothing. Avoid contact with eyes. Wear coveralls worn over short-sleeved shirt and short pants, socks and chemical resistant footwear and chemical resistant gloves (such as Nitrile, Butyl, Neoprene, and/or Barrier Laminate). Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash clothing before reuse.

3. The recommended statements of practical treatment are as follows:

IF SWALLOWED: Call a physician or Poison Control Center. Do not induce vomiting. Drink promptly a large quantity of milk, egg whites, gelatin solution, or if these are not available, drink large quantities of water. Avoid alcohol.

IF ON SKIN: Wash with plenty of soap and water. Get medical attention.

IF IN EYES: Flush eyes with plenty of water. Call a physician if irritation persists.

Note to Physician: Probable mucosal damage may contraindicate the use of gastric lavage.

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (81-3)

Product Manager: 21 **Reviewer**:M. Perry
MRID No.:441168-02 **Report Date**:3/5/96
Testing Laboratory:Product Safety Labs **Report No.**: 4185
Author(s): G. Wnorowski
Species:Rat
Weight: 226-251 g
Source:Hilltop Lab Animals
Test Material: Apron-FL
Quality Assurance (40 CFR 160.12):Present

Summary:

1. **LC_{50} (mg/kg)**: **Males**= --
Females= --
Combined= greater than 2.67 mg/L

2. **The estimated LC_{50} is greater than 2.67 mg/L.**

3. **Mean Concentration**: --

4. **Tox. Category**: IV **Classification**:Acceptable

Deviation From 81-3: None

Results:

Reported Mortality

Exposure Concentration mg/L	**(NUMBER KILLED/NUMBER TESTED)**		
	Males	**Females**	**Combined**
2.67	0/5	0/5	0/10

Avg. MMAD = 3.1 micrometers, GSD 1.66

Nominal Concentration = 50.05 mg/L

Clinical signs included facial staining, irregular respiration, hunched posture and hypoactivity. No significant findings were noted at necropsy.

DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (81-4)

Product Manager:21 **Reviewer**:M. Perry
MRID No.:266162 **Report Date**:8/25/86
Testing Laboratory:Food & Drug Research Labs
Report No.:9184B
Author(s): B. Busch
Species: Rabbit
Sex: --
Weight: --
Source: Ace Animals
Dosage: 0.1 ml
Test Material: Apron-FL
Quality Assurance (40 CFR 160.12):Present

Summary:

1. **Toxicity Category**: III
2. **Classification**: Acceptable

Deviations From 81-4: None

Results: Grade 1 to 2 redness, 1 to 3 chemosis, 0 to 1 opacity and no iritis were present during the first 72 hours post dose in the nonirrigated eyes. All irritation cleared in this group by 7 days.

DATA REVIEW FOR SKIN SENSITIZATION TESTING (81-6)

Product Manager:21
Reviewer:M. Perry
MRID No.:441168-03
Report Date:6/7/94
Testing Laboratory:Stillmeadow, Inc.
Report No.:1127-94
Author(s): J. Kuhn
Species:Guinea pig
Weight:415-495 g
Source: SASCO, Inc.
Test Material: Apron-FL
Positive Control Material: DNCB
Quality Assurance (40 CFR 160.12):Present

Method: Buehler

Summary:

1. **Classification**: Acceptable / Nonsensitizer

Deviation From 81-6: None

Results: Induction and challenge were performed with the undiluted liquid test material. The three induction applications failed to cause irritation. Following challenge, neither the test nor the naive control group exhibited a dermal reaction.

ACUTE TOX ONE-LINER

1. PC CODE: 113501

2. CURRENT DATE: 11/8/96

3. TEST MATERIAL: Metalaxyl 28.35%

Study/Species/Lab/ Study#/Date	MRID No.	Results	Tox. Cat.	Core Grade
81-3, Rat, Product Safety, 4185, 3/5/96	441168-02	LC50 greater than 2.0 mg/L	IV	A
81-4, Rabbit, Food & Drug Research, 9184B, 8/25/86	266162	Clear by 7 days	III	A
81-6, Guinea pig, Stillmeadow, Inc., 1127-94, 6/7/94	441168-03	Nonsensitizer	---	A

Core Grade Key:

A = Acceptable
S = Supplementary
U = Unacceptable